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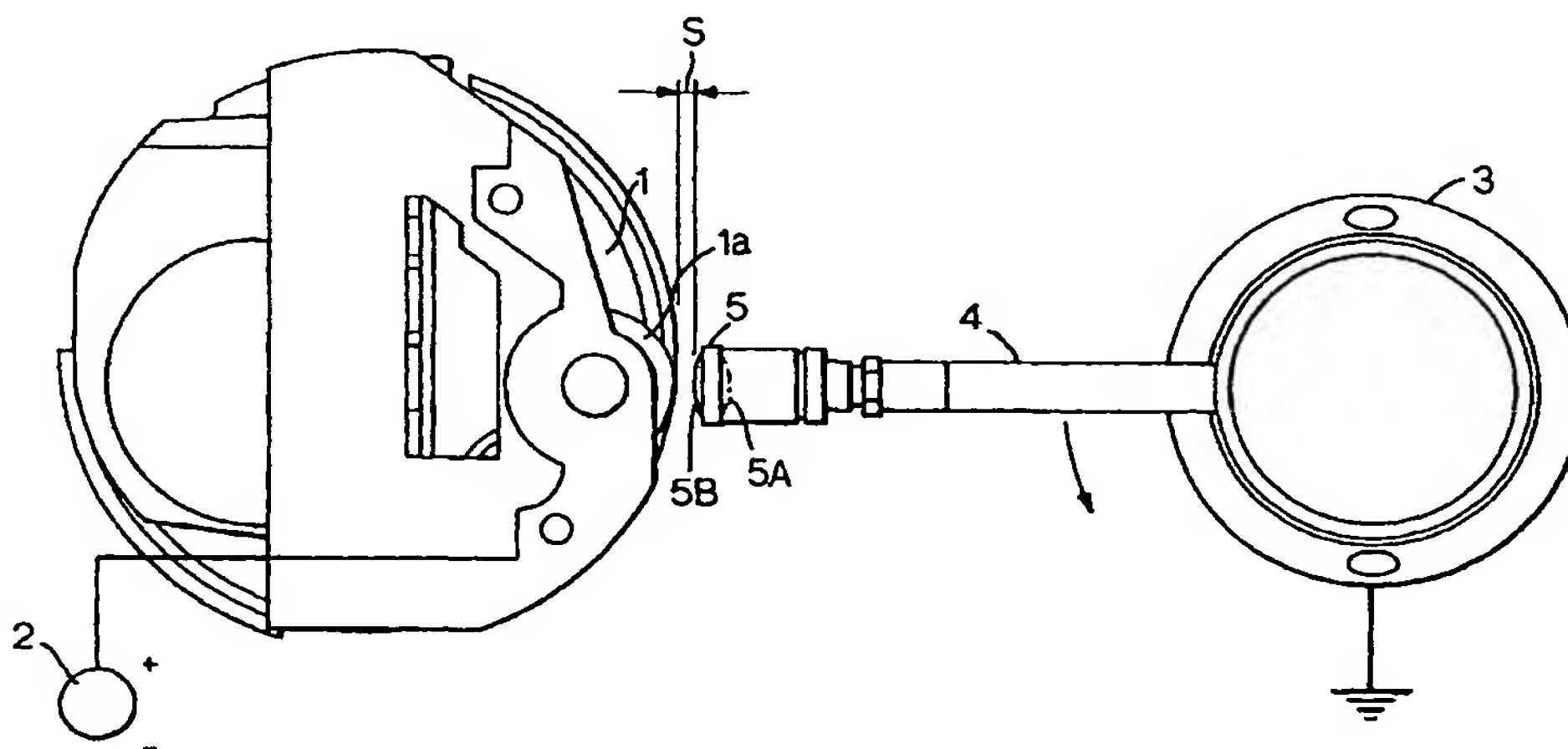
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- (71) Applicant (for all designated States except US): **PHOQUS LIMITED** [GB/GB]; 10 Kings Hill Avenue, West Malling, Kent ME19 4PQ (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **FEATHER, David**, Hoover [US/US]; 9899 Caminito Rogelio, San Diego, CA 92131 (US). **NELSON, Douglas, Howard** [US/US]; 1849 Paseo del Lago Vista, Carlsbad, CA 92083 (US).
- (74) Agents: **BARDO, Julian, Eason et al.**; Abel & Imray, 20 Red Lion Street, London WC1R 4PQ (GB).
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(54) Title: ELECTROSTATIC APPLICATION OF POWDER MATERIAL TO SOLID DOSAGE FORMS IN AN ELECTRIC FIELD



(57) Abstract: A method of electrostatically applying a powder material to a solid dosage form comprises the following steps: applying a bias voltage to generate an electric field between a source (1) of the powder material and the solid dosage form (5); applying an electrostatically charged powder material to the solid dosage form (5), the powder material being driven onto the solid dosage form (5) by the interaction of the electric field with the charged powder material, and the presence of the charged powder material on the solid dosage form serving to build up an electric charge on the solid dosage form (5) and thereby reduce the electric field generated by the bias voltage between the source (1) of powder material and the solid dosage form (5), and continuing the application of the electrostatically charged powder material to the solid dosage form (5) until the electric field between the source (1) of powder material and the solid dosage form (5) is so small that the driving of the powder material by the electric field onto the solid dosage form (5) is substantially terminated.

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Electrostatic Application of Powder Material to Solid Dosage
Forms in an Electric Field

The present invention relates to a method and apparatus
5 for the electrostatic application of powder material onto
the surfaces of solid dosage forms, and more particularly,
but not exclusively, pharmaceutical solid dosage forms.

A "solid dosage form" can be formed from any solid
material that can be apportioned into individual units; it
10 may be, but is not necessarily, an oral dosage form.
Examples of pharmaceutical solid dosage forms include
pharmaceutical tablets, pharmaceutical pessaries,
pharmaceutical bougies and pharmaceutical suppositories.
The term "pharmaceutical tablet" should be interpreted as
15 covering all pharmaceutical products which are to be taken
orally, including pressed tablets, pellets, capsules and
spherules. Examples of non-pharmaceutical solid dosage
forms include items of confectionery and washing detergent
tablets.

20 The electrostatic application of powder material to
solid dosage forms is known. In one technique, described in
WO 96/35516 powder material is applied onto the solid dosage
form while the solid dosage form is moving past a source of
the powder material. In this case the amount of powder
25 material applied to the solid dosage form depends upon the
speed at which the solid dosage form moves past the source
of powder material. In another technique, described in WO
96/39257, a predetermined amount of electrical charge is
deposited onto a solid dosage form and powder material of
30 opposite charge is brought to the solid dosage form, the
amount of powder material deposited on the solid dosage form
being the amount required to neutralise the charge
previously deposited; in that case the amount of powder

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material applied to the solid dosage form is dependent upon the amount of electrical charge deposited.

An advantage of employing electrostatic techniques to deposit powder material on a solid dosage form is the potential such techniques have for providing an even distribution of powder material over the surface of the solid dosage form. Thus it is desirable that an electrostatic technique in particular should enable an even distribution of powder material to be obtained; furthermore it is desirable if the total amount of powder despatched is consistent from one dosage form to the next. In the techniques referred to above it is difficult to obtain an even distribution and a consistent total amount of powder material deposition on each solid dosage form. Small changes in charges applied to the solid dosage form and/or the physical size and positioning of the solid dosage form, are liable to have a substantial effect on the deposition of the powder material on the solid dosage form.

The present invention provides a method of electrostatically applying a powder material to a solid dosage form, the method comprising the steps of:

- applying a bias voltage to generate an electric field between a source of the powder material and the solid dosage form;
- applying an electrostatically charged powder material to the solid dosage form, the powder material being driven onto the solid dosage form by the interaction of the electric field with the charged powder material and the presence of the charged powder material on the solid dosage form serving to build up an electric charge on the solid dosage form and thereby reduce the electric field generated by the bias voltage between the source of powder material and the solid dosage form, and

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continuing the application of the electrostatically charged powder material to the solid dosage form until the electric field between the source of powder material and the solid dosage form is so small that the driving of the powder material by the electric field onto the solid dosage form is substantially terminated.

In the method of the invention, the cancellation of an electric field initially provided between the source of the powder material and the solid dosage form, as a result of a build up of charge on the solid dosage form as charged powder material is deposited thereon, causes deposition of the powder to be terminated. The initial electric field may be provided by generating a selected bias voltage, enabling the size of the field to be controlled simply and reliably. Thereafter, provided the application of the charged powder material is continued until the driving effect of the electric field is substantially terminated, and provided the charging of the powder material is maintained at a constant level, the amount of powder material transferred to the solid dosage form is largely independent of the rate at which powder material is transferred to the solid dosage form; also, there may be relative movement of the solid dosage form past the source of the powder material as the powder material is applied to the solid dosage form, in which case if the speed of movement is slow enough for the driving effect of the electric field to be terminated before the spacing of the source of powder material and the solid dosage form are so great as to cease termination, the amount of powder material transferred to the solid dosage form is largely independent of the rate at which the solid dosage form is passed over the source of powder material.

During the method of the invention the shape of the electric field between the source of powder material and the

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solid dosage form may change; for example, in the case of application of powder to a domed surface of a solid dosage form, a first region of the solid dosage form may receive most of the charged powder material and, as that charged powder material builds up in the first region, the electric field may be reshaped so that a second region of the solid dosage form begins to receive most of the charged powder material. For each region, deposition of powder material will continue until the electric field between the source of powder material and the solid dosage form is so small that the driving of the powder material by the electric field onto the respective region is substantially terminated. The stage at which that termination point is reached is dependent principally on the amount of charge built up on the respective region of the solid dosage form, rather than on the distance between the respective region and the source of powder material. Thus, whilst the method of the invention may be employed to apply powder material to a planar surface of a solid dosage form with all parts of the planar surface substantially equispaced from the source of powder, the method is of special advantage when employed to apply material to a domed surface, for example the domed surface of one end face of a tablet. In such a case the central region of the domed surface may be closest to the source of powder material and the electric field initially created between the source of powder material and the tablet may drive the powder material principally onto the central region; as the central region becomes coated with powder material, however, the shape of the electric field changes and more powder material is applied to a peripheral region of the domed surface surrounding the central region; thus the method may provide a substantially even coating of powder material over a domed surface of a tablet, even

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though outer regions of the domed surface may be further from the source of powder material than a central region.

An important variable to control when carrying out the method of the invention is the voltage that generates the electric field; in the theoretical case where there is no leakage of charge and an electric field of unchanging shape extending between parallel planes of the source of powder material at the surface of the solid dosage form to be coated, the coating will continue until a sufficient mass per unit area of charged powder material has been applied to the surface of the solid dosage form to generate a potential at that surface of the same magnitude as the voltage that generates the electric field, whereby the electric field is completely cancelled out. Also, by changing, for example, the initial bias voltage, the mass per unit area of charged powder material required to cancel out the electric field will be changed and thus the thickness of the final powder layer applied can be altered.

The electric field is preferably provided by a bias voltage that initially lies in the range of 100V to 2000V and more preferably in the range of 200V to 1200V. If the bias voltage is very low, then a relatively small electric force is applied to the powder; if the force applied to the powder is very small, it may be difficult to apply the powder uniformly. If the bias voltage is very high, it may introduce a risk of discharge of the powder by dielectric breakdown or some other mechanism.

As will be understood, for a given size of gap the electric field is proportional to the potential difference between the source of powder material and the solid dosage form and the voltages referred to above are, strictly, the potential differences; in the usual case where the solid dosage forms are at earth potential the absolute potential

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of the bias voltage is also the potential difference, but in a case where the solid dosage form is maintained at a potential different from earth potential, it will be appreciated that the absolute bias potential will have a value chosen to provide a potential difference that is preferably within the ranges indicated above. For a given size of air gap there will be a maximum potential difference that can be applied before there is breakdown of the air.

The electric field is preferably provided by a bias voltage that is a steady DC voltage. The polarity of the bias voltage is chosen according to whether the powder is positively or negatively charged, which in turn is dependent upon the powder and/or the charging process employed: for negatively charged powders the bias voltage is negative and for positively charged powders it is positive, the bias voltage being defined as positive when the potential at the source of powder material is greater than the potential at the solid dosage form and vice versa. Preferably an alternating voltage, which is preferably substantially higher than the DC voltage, is superimposed on the initial bias voltage. The presence of such an alternating voltage serves to mobilise the charged powder reducing any tendency of the powder particles to adhere to an adjacent surface. The alternating voltage preferably has a peak to peak value greater than, and more preferably more than twice, the peak value of the DC bias voltage. For example the alternating voltage may have a peak to peak value of the order of 5kV. The sum of the DC bias voltage and one half of the peak to peak alternating voltage must not be so great that the potential difference causes breakdown of the air. The frequency of the alternating voltage is preferably in the range of 1 to 15kHz. In an example of the invention described below the frequency is within that range.

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The spacing between the source of powder material and the solid dosage form to which the powder material is applied is preferably in the range of 0.3mm to 5mm and more preferably in the range of 0.5mm to 2.0mm. If the spacing is relatively small by such standards then any variation from constant spacing between the solid dosage form and the source of powder material is likely to have a greater effect on the uniformity of deposition of the powder material. If the gap is increased by a small amount, one option is to keep the D.C. voltage at the same level and to increase the A.C. voltage; in that case substantially the same amount of powder material is applied before the electric field is cancelled. If the gap is increased to a greater extent, however, there will eventually be a need to increase the D.C. bias voltage. In that case a greater amount of powder will have to be applied before the field is cancelled, assuming that the amount of charge imparted to each unit mass of the powder material remains the same.

The thickness of the layer of powder material applied to the solid dosage form may be selected according to the particular requirements of a given product. Typically the thickness of the layer lies in the range of 10 to 50 μ m, although in some applications a greater thickness, for example up to 200 μ m may be desired; in some cases, such as where a large amount of an active powder material needs to be applied, a layer up to 1mm thick may be built up in a series of powder application steps.

In a case where there is relative movement of the solid dosage form past the source of powder material as the powder material is applied to the solid dosage form, it is important that there is an adequate time for the dosage form to be coated with sufficient powder material to reduce the electric field to a level such that powder material is no

longer driven onto the solid dosage form. Usually it will be preferable to reach that stage in a single pass of the solid dosage form past the source of powder material but it is also within the scope of the invention for the powder material to be applied in a plurality of discrete steps: for example, the powder material may be applied in a plurality of passes of the solid dosage form past the source of powder material or it may be applied by passing the solid dosage form past a plurality of sources of powder material. In the case where there are a plurality of sources of powder material, it is not necessary, especially if the same powder material is provided at each of the sources, for application of the powder material from each source to be continued until the electric field between the source and the solid dosage form is so small that the driving of the powder material onto the solid dosage form is substantially terminated; rather, that may apply for only one source, which is preferably the final source.

The aggregate time for which the application of the powder material to the solid dosage form must continue will be dependent upon the conditions under which the method is carried out, some of which have been discussed above. In a particular example of the invention described below the aggregate time required is about 400ms. Usually the aggregate time for which the powder material is applied to a given region of the solid dosage form is in the range of 50ms to 2s; as will now be understood, it is possible for the solid dosage form to be exposed to the charged powder material for considerably longer without significant further deposition of powder material, but more than a small amount of such time is wasteful. Consequently it is preferred that the aggregate time for which the given region of the solid

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dosage form is positioned adjacent to the source of powder material is in the range of 50ms to 2s.

When employing a plurality of sources of powder material to increase the aggregate time for which the powder material is applied to a given region of the solid dosage form, it may be convenient to provide substantially the same electrical conditions during each application stage, but that is not essential.

In the description above referring to a plurality of sources of powder material it will generally be the case that each source comprises the same powder material. That material may be, but need not be, an active material, for example a biologically active material, that is a material which increases or decreases the rate of a process in a biological environment. The biologically active material may be one which is physiologically active.

Another possibility is to provide a plurality of sources of powder material, each comprising a respective material. In that case a plurality of superimposed layers of material may be applied. Preferably the application of electrostatically charged powder material of each given material is continued until the electric field between the source of the powder and the solid dosage form is so small that the driving of the powder by the electric field onto the solid dosage form is substantially terminated. In that way, the amount of powder in each of the layers can be controlled. Preferably the application of a further layer of powder material from a further source involves the application of a higher initial bias voltage than applied during the application of a previous layer; as an alternative to increasing the electric field in this manner, steps may be taken to discharge the powder material

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previously applied to the solid dosage form, after which a further layer can be applied.

From the description above, it will be seen that the invention may be employed to apply a plurality of layers of powder material to a solid dosage form, each layer consisting of a selected amount of a selected powder material. That technique is especially, but not exclusively, useful in the production of what is commonly referred to as a controlled release or modified release solid dosage form. In such a case one, some or all of the layers may include active material. Thus dosage forms having two or more layers of different active material, with or without other intervening layers, may be employed.

Preferably the step of providing the electric field between the source of powder material and the solid dosage form comprises the step of providing respective electrically conducting members at the powder source and at the solid dosage form, and applying a potential difference between the electrically conducting members. Preferably the electrically conducting member at the powder source comprises an electrically conducting roller.

The powder material may be electrostatically charged in any suitable way. For example, it may be charged triboelectrically.

The solid dosage form may be a domed tablet having a pair of opposite domed end faces joined by a cylindrical side wall. In such a case, the electrostatically charged powder material may be applied uniformly over the whole of one domed end face of the tablet. The solid dosage form may, more particularly, be an oral dosage form and/or a pharmaceutical dosage form, for example a pharmaceutical tablet.

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Preferably, the method further comprises the step of treating the powder material to fix it on the solid dosage form. The treatment of the powder material to fix it to the solid dosage form preferably involves a heating step,
5 preferably using convection, but other forms of heating such as infra red radiation or conduction or induction may be used. The powder material should be heated to a temperature above its softening point, and then allowed to cool to a temperature below its glass transition temperature (T_g). It
10 is important to control the amount of heat applied to avoid degradation of the powder material and/or the solid dosage form. The amount of heat required may be reduced by applying pressure to the powder material. Alternatively, the powder material may include a polymer which is cured
15 during the treatment, for example, by irradiation with energy in the gamma, ultra violet or radio frequency bands.

The method may comprise the step of applying powder material to a first surface of the solid dosage form, and the subsequent step of applying powder material to a second
20 surface of the solid dosage form. Where the method is being used to apply a continuous coating to a solid dosage form, such a step will usually be necessary if the whole surface of the dosage form is to be coated.

Preferably, the method is carried out as a continuous
25 process.

The method of the present invention is not restricted to the use of any particular type of powder material. The powder materials described in WO 96/35413 are examples of suitable powder materials.

30 The powder material may include a biologically active material, that is, a material which increases or decreases the rate of a process in a biological environment. The

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biologically active material may be one which is physiologically active.

Conventionally, where an active material is to be administered in solid dosage form, the active material is mixed with a large volume of non-active "filler" material in order to produce a dosage form of manageable size. It has been found, however, that it is difficult to control accurately the amount of active material contained in each dosage form, leading to poor dose uniformity. That is especially the case where the required amount of active material in each dosage form is very low.

By electrostatically applying active material to a dosage form, it has been found to be possible to apply accurately very small amounts of active material to the dosage form, leading to improved dose reproducibility.

The powder material comprising active material may be applied to a solid dosage form containing the same or a different active material, or may be applied to a solid dosage form containing no active material.

The present invention also provides an apparatus for electrostatically applying a powder material to a solid dosage form, the apparatus being arranged to carry out the method defined above and comprising

a source of charged powder material,
a support for supporting a solid dosage form in the vicinity of the source of powder material,

a voltage source for generating an electric field between the source of powder material and a solid dosage form,

the apparatus being arranged such that electrostatically charged powder material is, in use, applied to the solid dosage form, the powder material being driven onto the solid dosage form by the interaction of the

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electric field with the charged powder material, the presence of the charged powder material on the solid dosage form serving to build up an electric charge on the solid dosage form and thereby reduce the electric field between the source of powder material and the solid dosage form, and the application of the electrostatically charged powder material to the solid dosage form is continued until the electric field between the source of powder material and the solid dosage form is so small that the driving of the powder material by the electric field onto the solid dosage form is substantially terminated.

The apparatus may be such that it is suitable for carrying out any of the methods referred to above.

By way of example, embodiments of the invention will now be described with reference to the accompanying drawings, of which:

Fig. 1 is a schematic side view of an apparatus for experimental use in the electrostatic application of powder material onto an end face of a tablet.

Fig 1 is a schematic drawing of an apparatus that we have used to implement the invention on a laboratory scale.

The apparatus generally comprises a source 1 of electrostatically charged powder material, connected to a variable voltage source 2, and a rotatable hub 3 from which an arm 4 projects radially, with a tablet 5 being carried on the free end of the arm 4. Powder material in the source 1 is fed to a roller 1a and is charged triboelectrically during its passage to the roller 1a. The roller 1a is electrically conducting and is connected to the voltage source 2. The hub 3 is electrically earthed and the arm 4 provides an electrical connection between a rear face 5A of the tablet 5 and earth.

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In use the hub 3 is rotated at a constant speed by an electric motor (not shown) causing the tablet 5 to pass through a region adjacent to the source 1 of powder material once for each revolution of the hub 3. When the tablet 5 is
5 closest to the powder material source 1, there is a spacing 'S' between the source 1 and a front face 5B of the tablet.

The apparatus has been used to carry out a variety of powder application processes, Examples of which will be given below.

10 In the Examples, the spacing 'S' between the source 1 and the front face 5B of the tablet was 1mm; the hub 3 was rotated at a constant speed of 0.9 r.p.m. resulting in a speed of movement of the tablet 5 past the powder material source 1 of 4.8mm/s leading to an effective "dwell time" of
15 the tablet face adjacent to the source 1 of 400mS.

The tablet 5 onto which powder material was supplied was of conventional shape having two domed end faces joined by a cylindrical side wall; the cylindrical side wall was of diameter 10mm and of height 2mm; the separation of the
20 domed end faces at their centres, where the separation was greatest, was 3.8mm. The tablet was a solid aluminium tablet of 6061-T6 aluminium.

The powder material provided at the source 1 was a material used as a toner in electrostatic photocopying,
25 namely that known as Optra C and sold by Lexmark. The particles of toner were generally of about 10µm diameter.

Example 1

The voltage source 2 was set to provide a DC bias
30 voltage initially of 500V with an AC voltage of 5000V peak to peak at 2kHz superimposed on the DC voltage. A tablet was mounted on the free end of the arm 4 and rotated by the hub 3 as described above at a speed of about 4.8mm/s. It

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was observed that during the first few passes the powder material at the source 1 was driven from the source onto the face 5B of the tablet 5 each time the tablet passed the source. The charge on the powder at the powder source was measured as approximately $7.2\mu\text{C/g}$, having been generated by triboelectric charging. In the example described both the charge on the powder and the voltage bias at the powder source were negative. The mass of powder on the tablet was measured after each pass and it was found that initially there was an approximately linear relationship between the number of passes of the tablet past the source and the amount of powder material applied to the tablet. Then the additional amount of powder applied during one further pass began to reduce and after 4 passes no further application of powder onto the tablet was detected. The total mass of powder material applied to the tablet at the end of the procedure was about 3.2mg provided by a layer of material of about 4.1mg/cm^2 . After 4 passes, when no further application of powder was detected, the voltage of the powder on the solid dosage form was renewed and found to be -490V.

Example 2

The same procedure was carried out as in Example 1 but in this case the initial DC bias voltage was 750V, with the AC voltage remaining at 5000V peak to peak at 2kHz. With the higher initial bias voltage, the rate of transfer of powder material was faster; after 5 passes, no further application of powder onto the tablet was detected. The total mass of powder material applied to the tablet at the end of the procedure was about 3.8mg, provided by a layer of material of about 4.9mg/cm^2 . The final voltage of the

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powder on the solid dosage form was measured and found to be -733V.

Examples 3 and 4

5 The same procedure as in Examples 1 and 2 was carried out, with further settings of the voltage source. The results of that, as well as the results from Examples 1 and 2 are tabulated below.

	DC Voltage V	AC Voltage at 2kHz (peak to peak) V	No. of passes before no increase in material deposit	Final mass of material transferred mg	Final voltage of material deposit
Example 1	-500	5000	4	3.2	-490
Example 2	-750	5000	5	3.8	-733
Example 3	-1000	5000	5	4.3	-971
Example 4	-250	5000	3	2.0	-243

10

A mass of 1mg of material transferred onto a tablet corresponds to a thickness of about 11.6 microns of the material on the tablet. Thus in the examples above the amounts of material transferred corresponds to thicknesses
15 on the tablet in the range of 23 to 50 microns.

When applying the invention on a commercial scale, the powder supply arrangement can still conveniently be as shown in Fig. 1. It is, however, preferable that the arrangement for conveying tablet cores past the powder supply
20 arrangement is able to convey a plurality of tablets, rather than just a single tablet as in the case of the apparatus shown in Fig. 1. Such conveying apparatus does not form part of the present invention and will not be described in detail in this specification. Examples of conveying
25 arrangements that may be employed are shown in WO 96/35516, WO 98/20861 and WO 98/20863, the contents of which are

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incorporated herein by reference. In the apparatus described in those documents, there is in each case one or more powder supply sources; for example, Fig. 2 of WO 98/20861 shows a powder supply source 16; as will be understood, the powder supply source 16 of WO 98/20861 may be replaced by the source 1 of Fig. 1 of the present invention to provide one example of a commercial apparatus embodying the invention. Also WO 96/34513, the contents of which are incorporated herein by reference, gives details of materials that may be employed in embodiments of the present invention.

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Claims

1. A method of electrostatically applying a powder material to a solid dosage form, the method comprising the
5 steps of:

applying a bias voltage to generate an electric field between a source of the powder material and the solid dosage form;

10 applying an electrostatically charged powder material to the solid dosage form, the powder material being driven onto the solid dosage form by the interaction of the electric field with the charged powder material, and the presence of the charged powder material on the solid dosage form serving to build up an electric charge on the solid
15 dosage form and thereby reduce the electric field generated by the bias voltage between the source of powder material and the solid dosage form, and

continuing the application of the electrostatically charged powder material to the solid dosage form until the
20 electric field between the source of powder material and the solid dosage form is so small that the driving of the powder material by the electric field onto the solid dosage form is substantially terminated.

2. A method according to claim 1, in which the electric
25 field is provided by a bias voltage that initially lies in the range of 100V to 2000V.

3. A method according to claim 2, in which the bias voltage initially lies in the range of 200V to 1200V.

4. A method according to any preceding claim, in which the
30 spacing between the source of powder material and the solid dosage form to which the powder material is applied is in the range of 0.3mm to 5mm.

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5. A method according to claim 4, in which the spacing between the source of powder material and the solid dosage form to which the powder material is applied is in the range of 0.5mm to 2.0mm.
- 5 6. A method according to any preceding claim, in which the electric field is provided by a bias voltage that is a steady DC voltage.
7. A method according to claim 6, in which an alternating voltage is superimposed on the bias voltage.
- 10 8. A method according to claim 7, in which the alternating voltage has a peak to peak value greater than the peak value of the DC bias voltage.
9. A method according to claim 8, in which the alternating voltage has a peak to peak value that is more than twice the
- 15 peak value of the DC bias voltage.
10. A method according to any preceding claim, in which the thickness of the layer of powder material applied to the solid dosage form lies in the range of 10 to 50 μ m.
11. A method according to any preceding claim, in which
- 20 there is relative movement of the solid dosage form past the source of powder material as the powder material is applied to the solid dosage form.
12. A method according to claim 11, in which the powder material is applied in a single pass of the solid dosage
- 25 form past the source of powder material.
13. A method according to claim 11, in which the powder material is applied in a plurality of passes of the solid dosage form past the source of powder material.
14. A method according to claim 11, in which the powder
- 30 material is applied by passing the solid dosage form over a plurality of sources of powder material.
15. A method according to any preceding claim, in which the aggregate time for which the powder material is applied to a

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given region of the solid dosage form is in the range of 50ms to 500ms.

16. A method according to any preceding claim, in which the aggregate time for which a given region of the solid dosage form is positioned adjacent to the source of powder material is in the range of 50ms to 2s.

17. A method according to any preceding claim in which a plurality of sources of powder material are provided, each comprising a respective material.

18. A method according to claim 17, in which the application of each electrostatically charged powder material is continued until the electric field between the source of the powder material and the solid dosage form is so small that the driving of the powder by the electric field onto the solid dosage form is substantially terminated.

19. A method according to claim 17 or 18, in which the application of a further layer of powder material from a further source involves the application of a higher initial bias voltage than applied during the application of a previous layer.

20. A method according to any preceding claim, in which the step of providing the electric field between the source of powder material and the solid dosage form comprises the step of providing respective electrically conducting members at the powder source and at the solid dosage form, and applying a potential difference between the electrically conducting members.

21. A method according to any preceding claim, in which the solid dosage form is a domed tablet having a pair of opposite domed end faces joined by a cylindrical side wall.

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22. A method according to claim 21, in which the electrostatically charged powder material is applied uniformly over the whole of a domed end face of the tablet.
23. A method according to any preceding claim, in which the
5 solid dosage form is an oral dosage form.
24. A method according to any preceding claim, in which the solid dosage form is a pharmaceutical dosage form.
25. A method according to claim 24, in which the pharmaceutical dosage form is a pharmaceutical tablet.
- 10 26. A method according to any preceding claim further comprising the step of treating the powder material to fix it on the solid dosage form.
27. A method according to claim 26, in which the treatment of the powder material to fix it on the solid dosage form
15 includes a heating step.
28. A method according to any preceding claim comprising the step of applying powder material to a first surface of the solid dosage form and the subsequent step of applying the material to a second surface of the solid dosage form.
- 20 29. A method according to any preceding claim, in which the powder material includes a biologically active material.
30. An apparatus for electrostatically applying a powder material to a solid dosage form, the apparatus including
a source of charged powder material,
25 a support for supporting a solid dosage form in the vicinity of the source of powder material,
a voltage source for applying a bias voltage between the source of powder material and a solid dosage form to generate an electric field therebetween,
30 the apparatus being arranged such that electrostatically charged powder material is, in use, applied to the solid dosage form, the powder material being driven onto the solid dosage form by the interaction of the

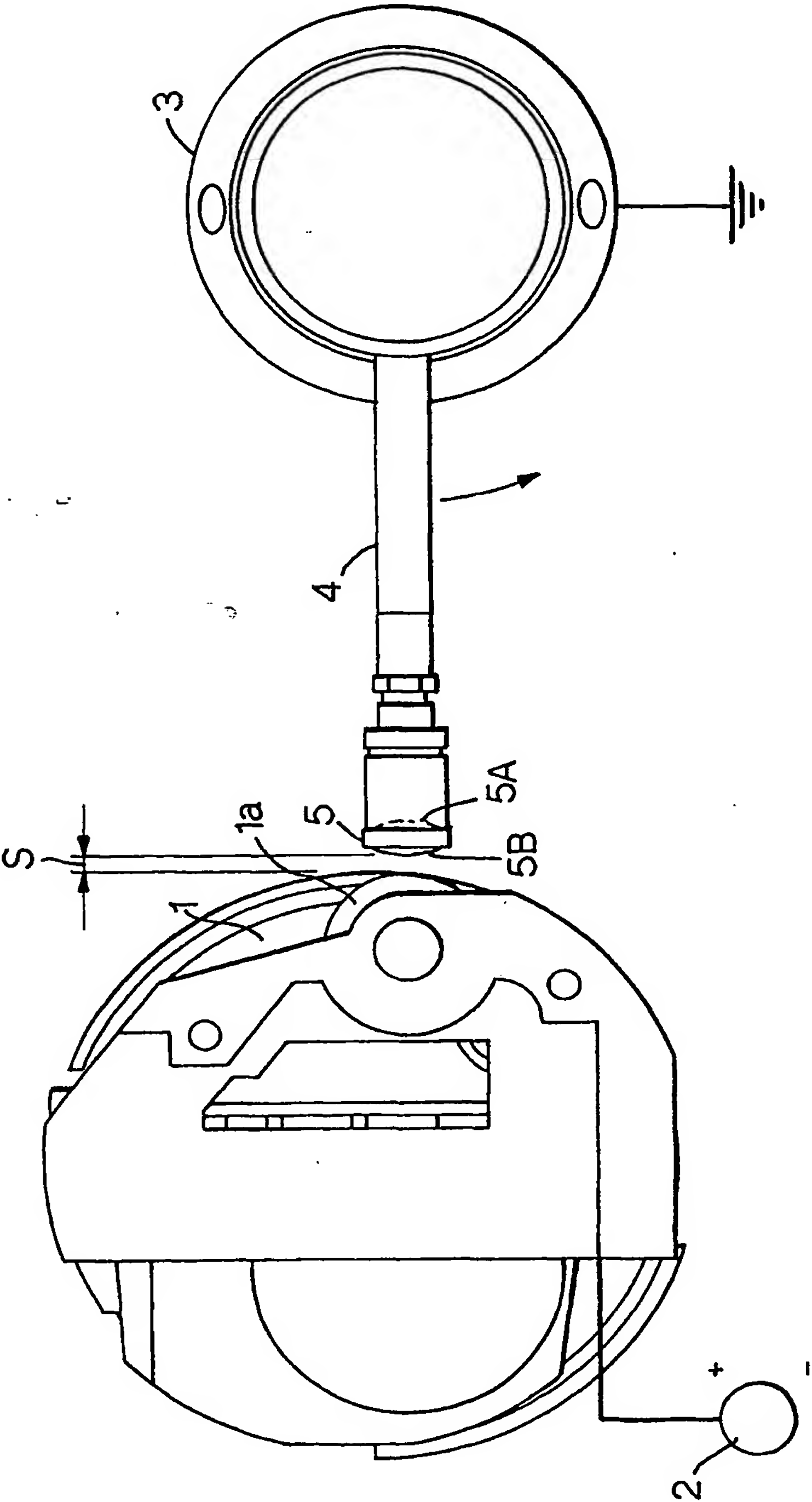
- 22 -

electric field generated by the bias voltage with the charged powder material, the presence of the charged powder material on the solid dosage form serving to build up an electric charge on the solid dosage form and thereby reduce the electric field between the source of powder material and the solid dosage form, and the application of the electrostatically charged powder material to the solid dosage form is continued until the electric field between the source of powder material and the solid dosage form is so small that the driving of the powder material by the electric field onto the solid dosage form is substantially terminated.

31. An apparatus according to claim 30, in which the apparatus is arranged to carry out a method according to any one of claims 2 to 29.

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Fig.1.



INTERNATIONAL SEARCH REPORT

In International Application No
PCT/GB 01/05744

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B05B5/08 A61K9/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 B05B A61K B05D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

PAJ, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 470 603 A (STANIFORTH JOHN N ET AL) 28 November 1995 (1995-11-28) column 1, line 38 - line 42 ---	1,6,11, 12,20, 23-25, 30,31
X	US 6 045 855 A (LINDQVIST ANDERS) 4 April 2000 (2000-04-04) column 4, line 6 - line 8 ---	1,6,11, 12,20, 23-25, 30,31
A	US 3 873 024 A (PROBST RICHARD O ET AL) 25 March 1975 (1975-03-25) column 7, line 53 - line 65 --- -/--	1,30

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

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- *G* document member of the same patent family

Date of the actual completion of the international search

8 April 2002

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Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Juguet, J

INTERNATIONAL SEARCH REPORT

Int onal Application No
PCT/GB 01/05744

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>US 5 354 583 A (ZUHR RAYMOND A ET AL) 11 October 1994 (1994-10-11) column 3, line 58 - line 68 -----</p>	1,30

INTERNATIONAL SEARCH REPORT

Information on patent family members

In International Application No

PCT/GB 01/05744

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5470603	A	28-11-1995	GB 2253164 A AT 126431 T AU 653989 B2 AU 1208492 A CA 2081921 A1 DE 69204127 D1 DE 69204127 T2 DK 526606 T3 EP 0526606 A1 ES 2078036 T3 WO 9214451 A1 GR 3018080 T3 HU 66848 A2 JP 2919971 B2 JP 5508337 T PL 296624 A1 US 5656080 A	02-09-1992 15-09-1995 20-10-1994 15-09-1992 23-08-1992 21-09-1995 04-04-1996 27-12-1995 10-02-1993 01-12-1995 03-09-1992 29-02-1996 30-01-1995 19-07-1999 25-11-1993 02-11-1993 12-08-1997
US 6045855	A	04-04-2000	SE 505906 C2 AU 1818997 A CN 1212639 A ,B EP 0881953 A1 JP 2000504626 T NO 983772 A SE 9600594 A WO 9729848 A1	20-10-1997 02-09-1997 31-03-1999 09-12-1998 18-04-2000 08-10-1998 03-03-1997 21-08-1997
US 3873024	A	25-03-1975	GB 1426536 A AU 473702 B AU 4121672 A BE 784862 A1 CA 964132 A1 CH 583592 A5 DE 2235752 A1 FR 2149752 A5 GB 1399934 A IT 960370 B JP 48028040 A NL 7210891 A	03-03-1976 01-07-1976 25-10-1973 02-10-1972 11-03-1975 14-01-1977 01-03-1973 30-03-1973 02-07-1975 20-11-1973 13-04-1973 15-02-1973
US 5354583	A	11-10-1994	US 5910220 A	08-06-1999